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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,915	05/10/2005	Gerd Haberhausen	21719-US	9560

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1637	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,915	HABERHAUSEN ET AL.	
	Examiner	Art Unit	
	STEPHANIE K. MUMMERT	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/23/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on November 29, 2007 is acknowledged and has been entered. Claims 1-7 have been amended. Claims 8-9 have been canceled. Claims 1-7 are pending.

Claims 1-7 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made FINAL as necessitated by amendment.

Previous Rejections

The objection to claims 4, 6 and 7 has been withdrawn in view of Applicant's amendment to the claims as filed with this reply. Applicant's original amendment to the claims with substitute specification filed May 10, 2005 is noted and the version of the claims filed with the substitute specification and as currently amended overcome the rejection of the claims. It is noted that the amendment to the claims filed with the preliminary amendment in addition to amendments to the specification should have been noted specifically in the document presented with the preliminary amendment for proper processing by the office.

The rejection of claims 2 and 3 under 35 U.S.C. 112, second paragraph as lacking antecedent basis is withdrawn in view of Applicant's amendment to the claims.

The rejection of claims 1-3 and 5 as being unpatentable over Greisen in view of deSilva is withdrawn in view of Applicant's amendment to the claims.

The rejection of claims 1-3 as being anticipated by Espy and Larson are withdrawn in view of Applicant's amendment to the claims.

The rejection of claims 1-3 and 5 as being obvious over Greisen in view of deSilva is withdrawn in view of Applicant's amendment to the claims.

Information Disclosure Statement

1. The information disclosure statement (IDS) submitted on January 23, 2008 was filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

New Grounds of Rejection necessitated by amendment

Claim Rejections - 35 USC § 103

2. Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jannes et al. (WO96/00298; January 1996, IDS reference) in view of de Silva et al. (Biochemica, 1998, no. 2, p. 12-15). Jannes teaches a method of amplification and detection of pathogenic organisms through the detection of the spacer region between the 16S and 23S rRNA gene (Abstract).

With regard to claim 1, Jannes teaches a method for identification of a pathogenic organism from a predetermined group of pathogens, comprising:

a) at least partially purifying nucleic acid from a clinical sample (Example 3, p. 78-83; alternatively, see Example 4, p. 84-86, p. 85 where clinical isolates were tested, see Table 7),

b) subjecting at least a first aliquot of said clinical specimen to at least a first amplification and detection reaction in one reaction vessel comprising:

ba) an amplification step using at least a first set of amplification primers capable of amplifying a pre-selected nucleic acid sequence comprising the 16s/23s rRNA spacer region from several or all members of said predetermined group of pathogens (p. 82-83 or p. 85, where clinical isolates were amplified using biotinylated primers and hybridized to 16s/23s rRNA spacer sequences in a reverse hybridization assay),

bb) a detection step using a plurality of hybridization reagents, said reagents together being capable of specifically detecting a pre-selected nucleic acid sequence comprising the 16s/23s rRNA spacer region from all members of said group of pathogens (p. 82-83 or p. 85, where clinical isolates were amplified using biotinylated primers and hybridized to 16s/23s rRNA spacer sequences in a reverse hybridization assay, see Table 5, 6 or 7 for hybridization results), said detection step comprising:

bba) monitoring hybridization of each of said hybridization reagents at a pre-selected temperature, said hybridization being indicative for at least the genus of said pathogen present in the sample (p. 82-83 or p. 85, where clinical isolates were amplified and hybridized to 16s/23s rRNA spacer sequences in a reverse hybridization assay, see Table 5, 6 or Table 7, where a variety of pathogens within a group were distinguished), and wherein said amplification and

detection reaction is indicative of the identity of said pathogenic organism from a predetermined group of pathogens (p. 85, where clinical isolates were amplified and hybridized to 16s/23s rRNA spacer sequences in a reverse hybridization assay, see Table 5, 6 or 7, where a variety of pathogens within a group were distinguished).

With regard to claim 2, Jannes teaches an embodiment of claim 1, further comprising subjecting at least a second aliquot of said clinical specimen to at least a second amplification and detection reaction in a different reaction vessel from said first aliquot of said clinical specimen being subjected to said first amplification and detection reaction in two different reaction vessels (Example 4, p. 84-86, where isolates were amplified in another aliquot for detection of C. trachomatis).

With regard to claim 3, Jannes teaches an embodiment of claim 2, further comprising subjecting at least a third aliquot of said clinical specimen to at least a third amplification and detection reaction in a different reaction vessel from said first aliquot of said clinical specimen being subjected to said first amplification and detection reaction, and said second aliquot of said clinical specimen being subjected to said second amplification and detection reaction (Example 6, p. 87, where clinical samples were amplified in another aliquot for detection of Mycobacterium).

With regard to claim 4, Jannes teaches an embodiment of claim 1, further comprising a hybridization reagent capable of specifically detecting an internal control (???).

With regard to claim 5, Jannes teaches an embodiment of claim 2, wherein gram positive pathogenic organisms are exclusively identified by said first amplification and detection reaction, and gram negative pathogenic organisms are exclusively identified by said second amplification

and detection reaction (Example 3, p. 78, where Listeria, a gram positive organism is detected; Example 4, p. 84-86, where C. trachomatis, a gram negative organism is detected).

With regard to claim 7, Jannes teaches an embodiment of claim 2, wherein said first amplification and detection reaction and said second amplification and detection reaction are performed with the same thermocycling profile (?).

Regarding claim 1, Jannes does not explicitly teach step bbb, wherein the temperature dependence of hybridization is monitored as indicative for at least the species of said pathogen.

With regard to claim 1, deSilva teaches an embodiment comprising bbb) monitoring temperature dependence of hybridization, said temperature dependence being indicative for at least the species of said pathogen (p. 14, Figures 3 and 5, where an example of monitoring temperature dependence of hybridization is depicted).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the methods taught by Jannes to incorporate the method of determining and monitoring the temperature dependence of hybridization as taught by deSilva to arrive at the claimed invention with a reasonable expectation for success. While Jannes teaches standard hybridization and detection of pathogenic sequences, it would have been prima facie obvious in view of the teachings of deSilva to monitor amplification using melting curve analysis to establish melting temperature as claimed and potentially to apply the sequence specific line probes used for detection of the rRNA spacer sequences to the LightCycler format of amplification and detection. As taught by deSilva, "sequence specific monitoring of PCR products is routinely performed by hybdiridization analysis using blots, gels, or microtiter plates. Hybridization of small oligonucleotide probes to template DNA can be visualized with

radioactively labeled probes, fluorescently labeled probes, or chemiluminescent techniques. These techniques, however, are time-consuming and can involve several handling steps that increase the risk of end-product contamination and sample tracking errors". This is in contrast to "Lightcycler is a microvolume fluorometer integrated with a thermal cycler that combines rapid-cycle PCR with real-time fluorescence monitoring" which allows "high throughput genotyping and product quantification" (p. 12). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have extended the methods taught by Jannes to incorporate the method of determining and monitoring the temperature dependence of hybridization as taught by deSilva to arrive at the claimed invention with a reasonable expectation for success.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jannes et al. (WO96/00298; January 1996) in view of de Silva et al. (Biochemica, 1998, no. 2, p. 12-15) as applied to claims 1-5 and 7 above, and further in view of Martin et al. (Journal of Clinical Microbiology, 2000, 38(10), p. 3735-3742). Jannes in view of deSilva teaches a method of amplification and detection of pathogenic organisms through the detection of the spacer region between the 16S and 23S rRNA gene (Abstract).

Jannes in view of de Silva teaches all of the limitations of claims 1-5 and 7 as recited in the 102 stated above. Jannes does not teach detection or identification of fungal pathogens. Martin teaches detection of fungal pathogens using line probe assays (Abstract).

With regard to claim 6, Martin teaches an embodiment of claim 3, wherein fungal pathogens are exclusively identified in said third amplification and detection reaction (Abstract, p. 3737, where the process of amplifying and detecting fungal pathogens is described in detail and comprises an additional reaction or aliquot).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the teachings of Jannes and de Silva to include the additional specific types of pathogens including fungal pathogens as taught by Martin to arrive at the claimed invention with a reasonable expectation for success. As taught by Martin, the study describes "universal amplification of the ITS region from fungi combined with the hybridization of the ITS PCR products to species specific oligonucleotide probes" (p. 3741, col. 1). Both Martin and Jannes share the internal transcribed spacer (ITS) as a target region (p. 3735). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have extended the teachings of Jannes and de Silva to include the additional specific types of pathogens including fungal pathogens as taught by Martin to arrive at the claimed invention with a reasonable expectation for success.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection

is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claim 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 6 of copending Application No. 10/534955 ('955 application) in view of Jannes et al. (WO96/00298; January 1996).

While these claims are not identical, they are not patentably distinct from one another. The claims of the copending '955 application are directed to a method for identification of a Gram positive pathogenic organism comprising amplification of a clinical sample, detecting amplification through hybridization, monitoring hybridization and identifying the organism(s). The claims of the instant application as amended are directed to a more narrow method of amplification and detection of pathogenic organisms comprising detection of a specific rRNA spacer region. In the copending application, claim 6 recites the detection of an rRNA spacer region. While the copending application does not specify the specific rRNA spacer sequence as comprising either 16S/23S or 18S/26S rRNA sequences, Jannes teaches specific detection of 16S/23S rRNA sequences. Considering the teaching by Jannes, "the spacer region situated between the 16S rRNA and the 23S rRNA gene, also referred to as the internal transcribed

spacer (ITS), is an advantageous target region for probe development for detection of pathogens of bacterial origin" (p. 1-2), therefore it would have been prima facie obvious that 16S/23S or 18S/26S rRNA sequences fall within the scope of the rRNA sequences claimed in the copending application.

Furthermore, in the instant application, gram positive bacteria are detected, however this limitation is recited as a dependent claim and as part of a method that comprises identification of both gram negative and gram positive bacteria. The similarities between these two copending applications, including the steps of monitoring temperature dependence of hybridization and using this hybridization detection to identify specific organisms, render the method of the instant application obvious.

This is a provisional obviousness-type double patenting rejection.

7. Claim 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/532319 ('319 application). While these claims are not identical, they are not patentably distinct from one another. The claims of the copending '319 application are directed to a method for detecting the presence of bacterial pathogens in clinical samples, comprising steps directed to the isolation of nucleic acids, amplification and quantifying the amount of nucleic acids comprising a sequence that is specific for a bacterial pathogen, wherein the method of quantification comprises amplification, monitoring of amplification through a hybridization probe and through monitoring temperature dependence of hybridization. The claims of the instant application are directed to a similar method directed to the amplification and detection of bacterial pathogens. The

differences between the current application and the '319 application lie in the specific recitation of analysis of specific aliquots of clinical specimens and comprising the use of multiple hybridization reagents in the instant application as contrasted with the real-time monitoring of amplification in the copending application, which falls within the scope of the amplification, detection and monitoring of temperature dependence of hybridization in the instant application. While the copending '319 application does not recite 16S/23S or 18S/26S rRNA spacer sequence, this preselected sequence of the instant application falls within the scope of the claim as recited in the copending application. Furthermore, while the copending application does not specify the specific rRNA spacer sequence as comprising either 16S/23S or 18S/26S rRNA sequences, Jannes teaches specific detection of 16S/23S rRNA sequences. Considering the teaching by Jannes, "the spacer region situated between the 16S rRNA and the 23S rRNA gene, also referred to as the internal transcribed spacer (ITS), is an advantageous target region for probe development for detection of pathogens of bacterial origin" (p. 1-2), therefore it would have been prima facie obvious that 16S/23S or 18S/26S rRNA sequences fall within the scope of the rRNA sequences claimed in the copending application.

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

Applicant's arguments with respect to claims 1-3 and 5 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie K. Mummert, Ph.D. whose telephone number is 571-272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stephanie K Mummert, Ph.D.
Examiner
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